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`UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte RAJESH V. MEHTA, RAMESH JAGANNATHAN,
SESHADRI JAGANANNATHAN, ROBERT A. ZABELNY,
ROSS A. SPROUT, and CARL R. BURNS

Appeal 2008-5096
Application 10/814,354
Technology Center 1700

Decided: November 25, 2008

Before THOMAS A. WALTZ, LINDA M. GAUDETTE, and
KAREN M. HASTINGS, *Administrative Patent Judges*.

WALTZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on an appeal under 35 U.S.C. § 134 from the Primary Examiner's final rejection of claims 1-8 and 10-18, which are the only claims pending in this application. We have jurisdiction pursuant to 35 U.S.C. § 6(b).

According to Appellants, the invention is directed to a process for the formation of nanoparticles of certain dimensions by use of Supercritical Anti-Solvent (SAS) precipitation with impeller mixing (App. Br. 1-2).

Further details of the invention may be gleaned from representative independent claim 1, reproduced below:

1. A process for the formation of particulate material of a desired substance comprising:

(i) charging a particle formation vessel, the temperature and pressure in which are controlled, with a supercritical fluid;

(ii) agitating the contents of the particle formation vessel with a rotary agitator comprising an impeller having an impeller surface and an impeller diameter, creating a relatively highly agitated turbulent flow zone located within a distance of one impeller diameter from the surface of the impeller of the rotary agitator, and a bulk mixing zone located at distances greater than one impeller diameter from the surface of the impeller;

(iii) introducing into the agitated particle formation vessel at least a first feed stream comprising at least a solvent and the desired substance dissolved therein through a first feed stream introduction port and a second feed stream comprising the supercritical, fluid through a second feed stream introduction port, wherein the desired substance is relatively insoluble in the supercritical fluid relative to its solubility in the solvent and the solvent is soluble in the supercritical fluid, and wherein the first and second feed stream introduction ports are located within a distance of one impeller diameter from the surface of the impeller of the rotary agitator such that the first and second feed streams are introduced into the highly agitated zone of the particle formation vessel and the first feed stream is dispersed in the supercritical fluid by action of the rotary agitator, allowing extraction of the solvent into the supercritical fluid, and

(iv) precipitating particles of the desired substance in the particle formation vessel with a volume-weighted average diameter of less than 20 nanometers.

The Examiner has relied on the following prior art references as evidence of obviousness:

Johnson	US 2004/0091546 A1	May 13, 2004

Saim	US 6,858,166 B2	Feb. 22, 2005
O'Connor	US 2006/0124783 A1	Jun. 15, 2006

ISSUES ON APPEAL

Claims 1-8 and 10-18 stand rejected under 35 U.S.C. § 103(a) as obvious over Saim in view of O'Connor and Johnson (Ans. 5).[1]

Appellants contend that the rejection represents clear error as the Examiner has misinterpreted the individual teachings of the cited references by combining the teachings of these references while each reference employs distinct types or materials and/or apparatuses for distinct purposes, and modifications of each reference go against the expressed preferences of the individual references (App. Br. 3).

Appellants contend that Saim teaches a rotary agitator, but does not teach that both the first and second streams should be introduced proximate to the highly agitated zone of the mixer (App. Br. 4). Appellants further contend that the Examiner's citations to Saim are clearly in error, and Saim teaches a preference for introduction of the pressurized gaseous fluid only from above an upper surface of the bed of carrier particles (*id.*). Appellants also contend that Saim is distinct from their invention since Appellants' claimed invention does not use any carrier particles (Reply Br. 2).

Appellants contend that Saim is directed to a specific result (coating of particles) that is different from O'Connor and Johnson (App. Br. 5). Appellants further contend that the physics of size reduction, such as in O'Connor, is fundamentally different from particle formation via

[1] The Examiner incorrectly includes previously cancelled claim 9 in the statement of the rejection on page 5 of the Answer (*see* App. Br. 1, which indicates that claim 9 has been cancelled). We hold this error harmless.

precipitation, as in Saim (*id.*). Appellants contend that Johnson is essentially duplicative of the acknowledged prior art mixing technique, but Johnson does not use SAS type particle formation or supercritical fluids (*id.,* citing Spec. 9:24-31, 10 and 11). Appellants assert that Johnson teaches that an agitator is not needed (App. Br. 6).

Finally, Appellants contend that any prima facie case of obviousness is overcome by the "surprising results of the present invention" (App. Br. 6). Appellants assert that Examples 4-8 in the Specification show production of particles with a mean diameter of less than 20 nm, while none of the references teach a process which enables such small particle size (*id.*).

The Examiner contends that all cited references are similarly directed towards particle precipitation processes for forming microparticles and nanoparticles utilized in the production of pharmaceutical products (Ans. 10).

The Examiner contends that Saim discloses introduction of first and second feed streams approximately within the highly agitated zone of the mixer/impeller (Ans. 5, 10). The Examiner also contends that Saim and O'Connor are both concerned with particle size reduction (Ans. 11).

The Examiner acknowledges that the teachings of Johnson were well known in the prior art mixing art, and both Johnson and Saim employ many similar features in their processes (Ans. 11).

Accordingly, we determine the following issues presented from the record in this appeal: (1) Have Appellants established that the Examiner committed reversible error in combining the teachings from Saim, O'Connor, and Johnson to establish a prima facie case of obviousness; and (2) if a prima facie case of obviousness has been established, have

Appellants overcome the prima facie case by a showing of unexpected results, namely Examples 4-8 from the Specification?

We determine that Appellants have not shown reversible error in the Examiner's determination and conclusion of prima facie obviousness, and Appellants have not met their burden of establishing unexpected results to overcome the prima facie obviousness. Therefore, for the reasons set forth in the Answer and those stated below, we sustain the sole ground of rejection presented for review in this appeal. Accordingly, the decision of the Examiner is AFFIRMED.

OPINION

We determine the following Findings of Fact (FF) from the record in this appeal:

(1) Saim discloses a method of small particle precipitation, followed by retention and dispersion of the particles onto or into a carrier material, where the particles are microparticles and nanoparticles (Ans. 5; Saim, Abstract; col. 14, ll. 65-66; col. 17, ll. 5-8);

(2) Saim teaches that "microparticles" preferably range from about 1 to 500 microns, while "nanoparticles" range from about 0.001 to 1 micron (Ans. 6; Saim, col. 9, ll. 36-41);[2]

(3) Saim discloses an embodiment termed "Mode 2," using steps (a)(2) and (b)(2), including introducing a first feed stream comprising a solvent and an active material through a first introduction port, introducing a second feed stream comprising the supercritical fluid through a second introduction port into the same

[2] The Examiner finds that 0.001 micron equals 1 nanometer (Ans. 6). This calculation is not disputed by Appellants (App. Br. 6).

region as the first feed stream, with both feed streams introduced approximately within a highly agitated mixing zone, where mixing is done by an impeller of unspecified diameter (Ans. 5; Saim, col. 10, ll. 49-52; col. 11, ll. 1-9; col. 12, ll. 25-36);

(4) Saim teaches that any conventional conditions (temperature, pressure, fluid flow rates, precipitation vessels, nozzle variations, etc.) that are commonly used in the art can be adjusted by a skilled technician to obtain the desired optimum performance (Ans. 5; Saim, col. 12, ll. 48-64);

(5) Saim teaches that the pressurized gaseous fluid is preferably pumped into the vessel from above the upper surface where the carrier powder bed is at rest, with the liquid solution preferably introduced into the vessel from a level below or slightly above the upper surface of the carrier powder bed at rest, and the carrier material bed is maintained in an agitated state such that the closeness of the feed spray and the stirring continuously recirculates carrier powder particles to prevent any substantial agglomeration; vigorous stirring can alleviate the need for fine atomized sprays of organic solutions in order to produce fine microparticles and nanoparticles (Ans. 5-6; Saim, col. 13, ll. 24-28; col. 14, ll. 46-66);

(6) Saim teaches that various mixing devices may be used, including impellers (Ans. 6; Saim, col. 14, l. 67-col. 15, l. 3);

(7) Saim teaches that one skilled in the art can easily adjust the distance between the mixed bed of carrier material and the introduction port for the gaseous fluid solution or liquid solution

to obtain the desired product, with distances disclosed anywhere from 0-12 inches, and Examples with two 4-blade pitched radial impellers and an introduction port 1 inch above the carrier bed (Saim, col. 15, ll. 7-13 and 22-27; Example 1 in col. 19; and Example 4 in col. 21);

(8) O'Connor discloses a process for reducing the median diameter of intermediate particles to obtain nanoparticles as small as 1-100 nanometers (nm) by use of a supercritical fluid, expansion, and various combinations of stirrers (Ans. 7; O'Connor, Abstract; ¶¶ [0001], [0003], [0010]-[0012], [0015], [0051], and [0052]);

(9) Johnson discloses a process of producing nanoparticles of less than 100 nm by flash precipitation, where the preferable region for the end of the outlet tube is near the mixer, since the size of the nanoparticles can be controlled by the mixing velocity and the location of the entry feeds (Ans. 7-8; Johnson, Abstract; Fig. 2; ¶¶ [0002], [0010], [0012], [0025], [0034]-[0035], [0083]);

(10) Johnson teaches that the process solvent and the non-process solvent should be introduced in a confined region where intimate mixing of the stream can occur rapidly with use of a mechanical agitator, with the region near the mechanical agitator having the desired greatest mixing velocity, preferably placing the incoming solvent stream directly into the region of high mixing velocity, with the preferred distance between the end of the inlet tube and the agitator tip within 15% of the agitator diameter (Ans. 7-8; Johnson, ¶¶ [0016]-[0017], [0041], [0044]).

Under 35 U.S.C. § 103, the factual inquiry into obviousness requires a determination of: (1) the scope and content of the prior art; (2) the differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) secondary considerations, if any (e.g., unexpected results). *See Graham v. John Deere Co.,* 383 U.S. 1, 17-18 (1966). "[I]f a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill." *KSR Int'l Co. v. Teleflex, Inc.,* 127 S. Ct. 1727, 1740 (2007). "[T]he analysis [of whether the subject matter of a claim is obvious] need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR,* 127 S. Ct. at 1740-41. "Under the correct analysis, any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed." *KSR,* 127 S. Ct. at 1741.

Applying the preceding legal principles to the Factual Findings (FF) on the record in this appeal, we determine that the Examiner has properly established a prima facie case of obviousness in view of the applied references. As shown by FFs (1), (2), (3), and (6) listed above, we determine that Saim discloses a process for the formation of nanoparticles as small as 1 nm in diameter by charging a vessel with a supercritical fluid, controlling the temperature and pressure, and agitating the first and second feed streams by use of a rotary agitator with an unspecified impeller diameter to form a highly agitated region. As shown by FFs (4), (5), and (7)

listed above, we determine that one of one of ordinary skill in this art would have easily optimized any process parameters to achieve the desired results, including optimizing the distance from the feed introduction ports to the impeller to achieve the desired vigorous stirring and alleviate the problem of agglomeration of particles. As correctly stated by the Examiner, any rotary agitator with impellers inherently agitates material in the immediate vicinity at a more agitated and vigorous rate than material at more distant location, thus producing the claimed turbulent flow zone and bulk mixing zone required by claim 1 on appeal (Ans. 5; *see* FF (3)).[3] This statement by the Examiner is also supported by the evidence from O'Connor (*see* FF (8)). We also note that Appellants acknowledge that prior art mixing technology employs inlet tubes which are within 15% of an agitator surface diameter, although this has not been done in an SAS type process (App. Br. 5). However, Appellants have not explained why one of ordinary skill in this art would not have recognized that this improvement could be employed in the same way in similar processes for the same advantage, i.e., better mixing. *See KSR,* 127 S. Ct. at 1740. As also shown by FFs (9) and (10) listed above, we determine that Johnson teaches advantageous results for introducing feed particles into a high mixing intensity zone to produce nanoparticles, specifically introducing particles at a distance within 15% of the agitator diameter from the agitator tip. As shown by FFs (3) and (5)

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[3] Appellants do not present any arguments directed to a separate claim. Thus, from the group of claims, we select claim 1 and decide the appeal with respect to the group of claims on the basis of this claim. *See* 37 C.F.R. § 41.37(c)(1)(vii).

listed above, we determine that Saim desires introducing the particle feed streams into a highly agitated, high intensity mixing zone.

For the foregoing reasons, we agree with the Examiner that it would have been obvious to one of ordinary skill in this art to employ two mixing zones in the process of Saim, while obtaining the desired highly agitated mixing zone by introducing particle feed streams within 15% of an agitator diameter from the tip of the agitator impeller, as taught by Johnson.

Appellants argue that Saim doesn't teach that both feed streams are introduced proximate to the highly agitated mixing zone, but teaches a preference for introduction of the pressurized gaseous fluid above the upper surface of the bed of carrier particles (App. Br. 4). This argument is not persuasive. As shown by FF (3) listed above, Saim teaches introduction of both feed streams approximately within the highly agitated mixing zone. Additionally, as shown by FF (5) and (7) listed above, Saim discloses introducing the spray solution close to the carrier material bed so that vigorous stirring can prevent agglomeration of particles while teaching that one of ordinary skill in this art can easily adjust the distance between the feed stream introduction ports and the carrier bed material to achieve the desired results, i.e., nanoparticle formation.

Appellants argue that the claimed invention does not use any carrier particles (Reply Br. 2). This argument is not well taken for two reasons. First, by the use of the transitional word "comprising," the claims do not exclude the use of carrier particles. *See Moleculon Research Corp. v. CBS,*

Inc., 793 F.2d 1261, 1271 (Fed. Cir. 1986).[4] Second, the carrier particles are only employed in the Saim process for retention of the nanoparticles (Saim, col. 1, ll. 9-14). Thus, the carrier bed particles are not essential to the formation of the nanoparticles.

Appellants contend that Saim is directed to coating of particles, and thus is different from O'Connor and Johnson (App. Br. 5). Appellants further contend that the physics of size reduction, as practiced by O'Connor, is fundamentally different from particle formation by precipitation, as found in Saim (*id.*). Appellants also contend that Johnson is not directed to an SAS type process, but uses conventional liquid solvents (*id.*). These arguments are not persuasive. As shown by FF (1) listed above, we determine that Saim is directed to the formation of nanoparticles. As discussed above, carrier material was only used to retain and disperse the nanoparticles. Since both Saim and O'Connor desire to reduce the size of the particles formed, we determine that one of ordinary skill in this art would have employed the advantages taught by O'Connor in the similar process of Saim. We also determine that one of ordinary skill in the art, aware of the desire in Saim to produce a highly agitated mixing zone for particulate material mixed by a rotary agitator impeller, would have employed the advantageous location for the introduction of the feed streams in relation to the impeller as taught by Johnson and known in the mixing art, regardless of the type of solvent employed.

Appellants assert that Examples 4-8 from the Specification show "surprising" results of particles with a mean diameter of less than 20 nm,

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[4] We note that Appellants teach that the particles obtained by the claimed process may be further coated on a substrate (Spec. 14:1-3).

while none of the references teaches a process which enables such a small particle size (App. Br. 6). Accordingly, we begin anew and consider all the evidence for and against patentability. *See In re Oetiker,* 977 F.2d 1443, 1445 (Fed. Cir. 1992). However, we do not find this evidence persuasive of non-obviousness. As shown by FFs (1) and (2) listed above, we determine that Saim discloses production of nanoparticles as small as 1 nm in diameter. Appellants have not shown that the enabling disclosure in Saim is deficient and that one of ordinary skill in this art could not produce nanoparticles as small as 1 nm in diameter by the Saim process. Therefore, we do not find any "surprising" results, much less unexpected results. Additionally, Examples 4-8 in the Specification are directed to specific particle materials processed under specific conditions while the claims are not so limited. Therefore, we determine that Appellants have not met their burden of explaining why these results are commensurate in scope with the subject matter sought to be patented. *See In re Dill,* 604 F.2d 1356, 1361 (CCPA 1979).

Based on the totality of the record, including due consideration of Appellants' arguments and evidence, we determine that the preponderance of the evidence weighs most heavily in favor of obviousness within the meaning of § 103. Accordingly, we sustain the sole ground of rejection presented for review in this appeal. The decision of the Examiner is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED

PL initials:
sld

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